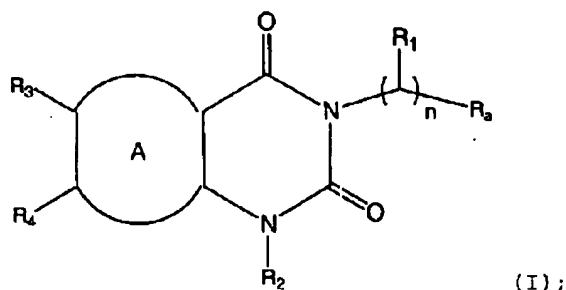


CLAIM AMENDMENTS

Please replace all prior versions and listings of claims with the amended claims as follows:

1. (Currently amended) A compound having formula (I):



wherein:

ring A is an ~~optionally-substituted~~ aryl or heteroaryl ring wherein said aryl or heteroaryl ring is either unsubstituted or substituted with one or more substituents selected from halogen, -R^o, -OR^o, -SR^o, 1,2-methylene-dioxy, 1,2-ethylenedioxy; unsubstituted phenyl (Ph), unsubstituted -O(Ph), unsubstituted -CH₂(Ph), unsubstituted -CH₂CH₂(Ph) or (Ph), -O(Ph), -CH₂(Ph), or -CH₂CH₂(Ph) substituted with one or more -R^o groups; -NO₂, -CN, -N(R^o)₂, -NR^oC(O)R^o, -NR^oC(O)N(R^o)₂, -NR^oCO₂R^o, -NR^oNR^oC(O)R^o, -NR^oNR^oC(O)N(R^o)₂, -NR^oNR^oCO₂R^o, -C(O)C(O)R^o, -C(O)CH₂C(O)R^o, -CO₂R^o, -C(O)R^o, -C(O)N(R^o)₂, -OC(O)N(R^o)₂, -S(O)₂R^o, -SO₂N(R^o)₂, -S(O)R^o, -NR^oSO₂N(R^o)₂, -NR^oSO₂R^o, -C(=S)N(R^o)₂, -C(=NH)-N(R^o)₂, or -(CH₂)_qNHC(O)R^o; wherein:

q is 0-2; and wherein:

each R^o is independently selected from hydrogen, a C₁₋₆ aliphatic, wherein said C₁₋₆ aliphatic group is either unsubstituted or substituted with one or more

substituents selected from =O, =S, =NNHR^{*}, =NN(R^{*})₂, =NNHC(O)R^{*}, =NNHCO₂(alkyl), =NNHSO₂(alkyl), =NR^{*}NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, halogen, C₁₋₄ aliphatic, OH, O(C₁₋₄ aliphatic), NO₂, CN, CO₂H, CO₂(C₁₋₄ aliphatic), O(halo C₁₋₄ aliphatic), or halo C₁₋₄ aliphatic; an unsubstituted 5-6 membered heteroaryl or heterocyclic ring, phenyl, -O(Ph), or -CH₂(Ph), or wherein two occurrences of R^{*}, on the same substituent or different substituents, taken together, form a 5-8-membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein:

each R^{*} is independently selected from hydrogen or a C₁₋₆ aliphatic group wherein said aliphatic group of R^{*} is either unsubstituted or substituted with one or more substituents selected from NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, halogen, C₁₋₄ aliphatic, OH, O(C₁₋₄ aliphatic), NO₂, CN, CO₂H, CO₂(C₁₋₄ aliphatic), O(halo C₁₋₄ aliphatic), or halo(C₁₋₄ aliphatic);

the nitrogen of any non-aromatic heterocyclic ring is either unsubstituted or substituted with one or more groups selected from -R^{*}, -N(R^{*})₂, -C(O)R^{*}, -OR^{*}, -CO₂R^{*}, -C(O)C(O)R^{*}, -C(O)CH₂C(O)R^{*}, -SO₂R^{*}, -SO₂N(R^{*})₂, -C(=S)N(R^{*})₂, -C(=NH)-N(R^{*})₂, or -NR^{*}SO₂R^{*}; wherein:

R^{*} is hydrogen, an unsubstituted 5-6 membered heteroaryl or heterocyclic ring, an unsubstituted C₁₋₆ aliphatic, unsubstituted phenyl (Ph), unsubstituted -O(Ph), unsubstituted -CH₂(Ph), unsubstituted -CH₂CH₂(Ph); or C₁₋₆ aliphatic, phenyl(Ph), -O(Ph), -CH₂(Ph), or -CH₂CH₂(Ph) substituted with one or more groups selected from NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, halogen, C₁₋₄ aliphatic, OH, O(C₁₋₄ aliphatic), NO₂, CN, CO₂H, CO₂(C₁₋₄ aliphatic), O(halo C₁₋₄ aliphatic), or halo(C₁₋₄ aliphatic) or wherein two occurrences of R^{*}, on the same substituent or different substituents, taken together, form a 5-8-membered heterocyclyl or heteroaryl ring

having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

R_a is -COOH;

n is 0-4;

R_1 is H, or ~~an optionally substituted a~~
hydroxyaliphatic, aminoaliphatic, aliphatic-COOH,
aliphatic-CONH₂, or arylaliphatic wherein said
hydroxyaliphatic, aminoaliphatic, aliphatic-COOH,
aliphatic-CONH₂, or arylaliphatic is either unsubstituted
or substituted with one or more substituents selected
from halogen, -R^o, -OR^o, -SR^o, 1,2-methylene-dioxy, 1,2-
ethylenedioxy; unsubstituted phenyl (Ph), unsubstituted
-O(Ph), unsubstituted -CH₂(Ph), unsubstituted -CH₂CH₂(Ph)
or (Ph), -O(Ph), -CH₂(Ph), or -CH₂CH₂(Ph) substituted with
one or more -R^o groups; -NO₂, -CN, -N(R^o)₂, -NR^oC(O)R^o,
-NR^oC(O)N(R^o)₂, -NR^oCO₂R^o, -NR^oNR^oC(O)R^o, -NR^oNR^oC(O)N(R^o)₂,
-NR^oNR^oCO₂R^o, -C(O)C(O)R^o, -C(O)CH₂C(O)R^o, -CO₂R^o, -C(O)R^o,
-C(O)N(R^o)₂, -OC(O)N(R^o)₂, -S(O)₂R^o, -SO₂N(R^o)₂, -S(O)R^o,
-NR^oSO₂N(R^o)₂, -NR^oSO₂R^o, -C(=S)N(R^o)₂, -C(=NH)-N(R^o)₂, or
-(CH₂)_qNHC(O)R^o; wherein:

q is 0-2; and wherein:

each R^o is independently selected from hydrogen, a
C₁₋₆ aliphatic, wherein said C₁₋₆ aliphatic group is either
unsubstituted or substituted with one or more
substituents selected from =O, =S, =NNHR^o, =NN(R^o)₂,
=NNHC(O)R^o, =NNHCO₂(alkyl), =NNHSO₂(alkyl), =NR^oNH₂, NH(C₁₋₄
aliphatic), N(C₁₋₄ aliphatic)₂, halogen, C₁₋₄ aliphatic,
OH, O(C₁₋₄ aliphatic), NO₂, CN, CO₂H, CO₂(C₁₋₄ aliphatic),
O(halo C₁₋₄ aliphatic), or halo C₁₋₄ aliphatic; an
unsubstituted 5-6 membered heteroaryl or heterocyclic
ring, phenyl, -O(Ph), or -CH₂(Ph), or wherein two
occurrences of R^o, on the same substituent or different
substituents, taken together, form a 5-8-membered
heterocyclyl or heteroaryl ring having 1-3 heteroatoms

independently selected from nitrogen, oxygen, or sulfur;
wherein:

each R' is independently selected from hydrogen or
a C₁₋₆ aliphatic group wherein said aliphatic group of R'
is either unsubstituted or substituted with one or more
substituents selected from NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄
aliphatic)₂, halogen, C₁₋₄ aliphatic, OH, O(C₁₋₄
aliphatic), NO₂, CN, CO₂H, CC₂(C₁₋₄ aliphatic), O(halo C₁₋₄
aliphatic), or halo(C₁₋₄ aliphatic);

the nitrogen of any non-aromatic heterocyclic ring
is either unsubstituted or substituted with one or more
groups selected from -R⁺, -N(R⁺)₂, -C(O)R⁺, -OR⁺, -CO₂R⁺,
-C(O)C(O)R⁺, -C(O)CH₂C(O)R⁺, -SO₂R⁺, -SO₂N(R⁺)₂,
-C(=S)N(R⁺)₂, -C(=NH)-N(R⁺)₂, or -NR⁺SO₂R⁺; wherein:

R⁺ is hydrogen, an unsubstituted 5-6 membered
heteroaryl or heterocyclic ring, an unsubstituted C₁₋₆
aliphatic, unsubstituted phenyl (Ph), unsubstituted
-O(Ph), unsubstituted -CH₂(Ph), unsubstituted -CH₂CH₂(Ph);
or C₁₋₆ aliphatic, phenyl (Ph), -O(Ph), -CH₂(Ph), or
-CH₂CH₂(Ph) substituted with one or more groups selected
from NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, halogen,
C₁₋₄ aliphatic, OH, O(C₁₋₄ aliphatic), NO₂, CN, CO₂H, CO₂(C₁₋
₄ aliphatic), O(halo C₁₋₄ aliphatic), or halo(C₁₋₄
aliphatic) or wherein two occurrences of R⁺, on the same
substituent or different substituents, taken together,
form a 5-8-membered heterocyclyl or heteroaryl ring
having 1-3 heteroatoms independently selected from
nitrogen, oxygen, or sulfur;

R₂ is an optionally substituted aliphatic,
arylaliphatic, cycloaliphatic-aliphatic, or
heteroarylaliphatic, ~~or heterocyclaliphatic~~, wherein
said aliphatic, cycloaliphatic-aliphatic,
heteroarylaliphatic, or is either unsubstituted or
substituted with one or more substituents selected from
halogen, -R^o, -OR^o, -SR^o, 1,2-methylene-dioxy, 1,2-
ethylenedioxy; unsubstituted phenyl (Ph), unsubstituted

-O(Ph), unsubstituted -CH₂(Ph), unsubstituted -CH₂CH₂(Ph) or (Ph), -O(Ph), -CH₂(Ph), or -CH₂CH₂(Ph) substituted with one or more -R° groups; -NO₂, -CN, -N(R°)₂, -NR°C(O)R°, -NR°C(O)N(R°)₂, -NR°CO₂R°, -NR°NR°C(O)R°, -NR°NR°C(O)N(R°)₂, -NR°NR°CO₂R°, -C(O)C(O)R°, -C(O)CH₂C(O)R°, -CO₂R°, -C(O)R°, -C(O)N(R°)₂, -OC(O)N(R°)₂, -S(O)₂R°, -SO₂N(R°)₂, -S(O)R°, -NR°SO₂N(R°)₂, -NR°SO₂R°, -C(=S)N(R°)₂, -C(=NH)-N(R°)₂, or -(CH₂)_qNHC(O)R°; wherein:

q is 0-2; and wherein:

each R° is independently selected from hydrogen, a C₁₋₆ aliphatic, wherein said C₁₋₆ aliphatic group is either unsubstituted or substituted with one or more substituents selected from =O, =S, =NNHR°, =NN(R°)₂, =NNHC(O)R°, =NNHCO₂(alkyl), =NNHSO₂(alkyl), =NR°NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, halogen, C₁₋₄ aliphatic, OH, O(C₁₋₄ aliphatic), NO₂, CN, CO₂H, CO₂(C₁₋₄ aliphatic), O(halo C₁₋₄ aliphatic), or halo C₁₋₄ aliphatic; an unsubstituted 5-6 membered heteroaryl or heterocyclic ring, phenyl, -O(Ph), or -CH₂(Ph), or wherein two occurrences of R°, on the same substituent or different substituents, taken together, form a 5-8-membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein:

each R' is independently selected from hydrogen or a C₁₋₆ aliphatic group wherein said aliphatic group of R' is either unsubstituted or substituted with one or more substituents selected from NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, halogen, C₁₋₄ aliphatic, OH, O(C₁₋₄ aliphatic), NO₂, CN, CO₂H, CO₂(C₁₋₄ aliphatic), O(halo C₁₋₄ aliphatic), or halo(C₁₋₄ aliphatic);

the nitrogen of any non-aromatic heterocyclic ring is either unsubstituted or substituted with one or more groups selected from -R', -N(R')₂, -C(O)R', -OR', -CO₂R', -C(O)C(O)R', -C(O)CH₂C(O)R', -SO₂R', -SO₂N(R')₂.

-C(=S)N(R⁺)₂, -C(=NH)-N(R⁺)₂, or -NR⁺SO₂R⁺; wherein:
R⁺ is hydrogen, an unsubstituted 5-6 membered heteroaryl
or heterocyclic ring, an unsubstituted C₁₋₆ aliphatic,
unsubstituted phenyl (Ph), unsubstituted -O(Ph),
unsubstituted -CH₂(Ph), unsubstituted -CH₂CH₂(Ph); or C₁₋₆
aliphatic, phenyl(Ph), -O(Ph), -CH₂(Ph), or -CH₂CH₂(Ph)
substituted with one or more groups selected from NH₂,
NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, halogen, C₁₋₄
aliphatic, OH, O(C₁₋₄ aliphatic), NO₂, CN, CO₂H, CO₂(C₁₋₄
aliphatic), O(halo C₁₋₄ aliphatic), or halo(C₁₋₄ aliphatic)
or wherein two occurrences of R⁺, on the same substituent
or different substituents, taken together, form a 5-8-
membered heterocyclyl or heteroaryl ring having 1-3
heteroatoms independently selected from nitrogen, oxygen,
or sulfur;

R³ and R⁴ are independently selected from R¹¹, R¹²,
 R¹⁴ or R¹⁵;

wherein:

each R¹¹ is independently selected from 1,2-
 methylenedioxy, 1,2-ethylenedioxy, R⁶ or (CH₂)_m-Y;

wherein m is 0, 1 or 2; and

Y is selected from halogen, CN, NO₂, CF₃,
 OCF₃, OH, SR⁶, S(O)R⁶, SO₂R⁶, NH₂, NHR⁶, N(R⁶)₂, NR⁶R⁸,
 COOH, COOR⁶ or OR⁶;

each R¹² is independently selected from
 (C₁-C₆)-straight or branched alkyl, or (C₂-C₆)-straight
 or branched alkenyl or alkynyl; and each R¹² optionally
 comprises up to 2 substituents, wherein:

the first of said substituents, if
 present, is selected from R¹¹, R¹⁴ and R¹⁵, and

the second of said substituents, if
 present, is R¹¹;

each R¹⁴ is independently selected from OR¹⁵,

OC(O)R^6 , OC(O)R^{15} , OC(O)OR^6 , OC(O)OR^{15} , $\text{OC(O)N(R}^6)_2$,
 $\text{OP(O)(OR}^6)_2$, SR^6 , SR^{15} , S(O)R^6 , S(O)R^{15} , SO_2R^6 , SO_2R^{15} ,
 $\text{SO}_2\text{N(R}^6)_2$, $\text{SO}_2\text{NR}^{15}\text{R}^6$, SO_3R^6 , C(O)R^{15} , C(O)OR^{15} , C(O)R^6 ,
 C(O)OR^6 , NC(O)C(O)R^6 , NC(O)C(O)R^{15} , NC(O)C(O)OR^6 ,
 $\text{NC(O)C(O)N(R}^6)_2$, $\text{C(O)N(R}^6)_2$, $\text{C(O)N(OR}^6)\text{R}^6$, $\text{C(O)N(OR}^6)\text{R}^{15}$,
 $\text{C(NOR}^6)\text{R}^6$, $\text{C(NOR}^6)\text{R}^{15}$, $\text{N(R}^6)_2$, $\text{NR}^6\text{C(O)R}^{11}$, $\text{NR}^6\text{C(O)R}^6$,
 $\text{NR}^6\text{C(O)R}^{15}$, $\text{NR}^6\text{C(O)OR}^6$, $\text{NR}^6\text{C(O)OR}^{15}$, $\text{NR}^6\text{C(O)N(R}^6)_2$,
 $\text{NR}^6\text{C(O)NR}^{15}\text{R}^6$, $\text{NR}^6\text{SO}_2\text{R}^6$, $\text{NR}^6\text{SO}_2\text{R}^{15}$, $\text{NR}^6\text{SO}_2\text{N(R}^6)_2$,
 $\text{NR}^6\text{SO}_2\text{NR}^{15}\text{R}^6$, $\text{N(OR}^6)\text{R}^6$, $\text{N(OR}^6)\text{R}^{15}$, $\text{P(O)(OR}^6)\text{N(R}^6)_2$, and
 $\text{P(O)(OR}^6)_2$;

each R^{15} is a cycloaliphatic, aryl, heterocyclyl, or heteroaromatic; and each R^{15} optionally comprises up to 3 substituents, each of which, if present, is R^{11} ;

each R^6 is independently selected from H, $(\text{C}_1\text{-C}_6)$ -straight or branched alkyl, or $(\text{C}_2\text{-C}_6)$ straight or branched alkenyl; and each R^6 optionally comprises a substituent that is R^7 ;

R^7 is a cycloaliphatic, aryl, heterocyclyl, or heteroaromatic; and each R^7 optionally comprises up to 2 substituents independently chosen from H, $(\text{C}_1\text{-C}_6)$ -straight or branched alkyl, $(\text{C}_2\text{-C}_6)$ straight or branched alkenyl, 1,2-methylenedioxy, 1,2-ethylenedioxy, or $(\text{CH}_2)_p\text{-Z}$;

wherein p is 0, 1 or 2; and

Z is selected from halogen, CN , NO_2 , CF_3 , OCF_3 , OH , $\text{S}(\text{C}_1\text{-C}_6)\text{-alkyl}$, $\text{SO}(\text{C}_1\text{-C}_6)\text{-alkyl}$, $\text{SO}_2(\text{C}_1\text{-C}_6)\text{-alkyl}$, NH_2 , $\text{NH}(\text{C}_1\text{-C}_6)\text{-alkyl}$, $\text{N}((\text{C}_1\text{-C}_6)\text{-alkyl})_2$, $\text{N}((\text{C}_1\text{-C}_6)\text{-alkyl})\text{R}^8$, COOH , $\text{C(O)O}(\text{C}_1\text{-C}_6)\text{-alkyl}$ or $\text{O}(\text{C}_1\text{-C}_6)\text{-alkyl}$; and

R^8 is an amino protecting group;

provided that:

- R^3 and R^4 are not simultaneously hydrogen;
when R^3 is H, then R^4 is not chloro; and
when R^4 is H, then R^3 is not $-SCH_3$ or $-NH-C(O)CH_3$.

2. (Original) The compound according to claim 1, wherein ring A is an optionally substituted 5 or 6 membered aryl or heteroaryl ring, wherein said heteroaryl ring contains up to 2 ring heteroatoms independently selected from O, S, or NH.

3. (Original) The compound according to claim 2, wherein ring A is phenyl.

4. (Original) The compound according to claim 1, wherein R_1 is hydrogen, $-(CH_2)_q-X$, wherein q is 1-4, and X is OH, NH_2 , COOH or $CONH_2$, (C1-C6)-alkyl, or benzyl.

5. (Currently amended) The compound according to claim 4, wherein R_1 is hydrogen, hydroxymethyl, methyl, $-CH_2COOH$, $-CH_2CONH_2$, aminobutyl, ~~methyl~~, or isopentyl.

6. (Currently amended) The compound according to claim 1, wherein R_2 is selected from butyl, isobutyl, methoxypropyl, cyclopentyl, cyclohexylmethyl, ~~or phenyl~~, ~~trifluorophenyl~~, ~~benzyl~~, ~~fluorobenzyl~~, ~~methylenedioxybenzyl~~, pyridylmethyl, furanylmethyl, ~~tetrahydrofuranylmethyl~~, ~~N-morpholinylmethyl~~, ~~thienylmethyl~~, ~~2-oxo-pyrrolidinylpropyl~~, ~~phenylethyl~~, ~~chlorophenylethyl~~, ~~methoxyphenylethyl~~, ~~or~~ ~~dimethoxyphenylethyl~~.

7. (Currently amended) The compound according to claim 6, wherein R_2 is selected from 2-furanylmethyl ~~or~~ ~~methyl~~.

~~According to another preferred embodiment, R₃ and R₄ are independently selected from hydrogen, halo, acetamido, allyloxy, thiophenyl, sulfox, alkyl, or sulfoxyphenyl.~~

8. (Canceled)

9. (Currently amended) A pharmaceutical composition comprising a compound according to any one of claims ~~4-8~~ 1-7 and 17-18 and a pharmaceutically acceptable adjuvant or carrier.

10. (Withdrawn) A method for treating or lessening the severity of a disease in a patient, wherein said disease is selected from autoimmune diseases, proliferative diseases, angiogenic disorders, or cancers, said method comprising the step of administering to said patient a composition according to claim 9.

11. (Withdrawn) A method for treating or lessening the severity of a SHP-2-mediated disease or condition in a patient comprising the step of administering to said patient a composition according to claim 9.

12. (Withdrawn) The method according to claim 10, wherein said autoimmune disease is selected from glomerulo-nephritis, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, chronic thyroiditis, Graves' disease, autoimmune gastritis, diabetes, autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, atopic dermatitis, chronic active hepatitis, myasthenia gravis, multiple sclerosis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, psoriasis, or graft vs. host disease.

13. (Withdrawn) The method according to claim 10, wherein said proliferative disease is selected from acute

myelogenous leukemia, chronic myelogenous leukemia, metastatic melanoma, Kaposi's sarcoma, multiple myeloma or HTLV-1-mediated tumorigenesis.

14. (Withdrawn) The method according to claim 10, wherein said angiogenic disorder is selected from solid tumors, ocular neovascularization, or infantile haemangiomas.

15. (Withdrawn) The method according to claim 10, wherein said cancers is selected from colon cancer, breast cancer, stomach cancer, or ovarian cancers.

16. (Withdrawn-currently amended) An implantable medical device coated with a compound according to any one of claims ~~1-8~~ 1-7 and 17-18, wherein said device is selected from prostheses, artificial valves, vascular grafts, stents or catheters.

17. (New) The compound according to claim 1 wherein R_3 and R_4 are independently selected from hydrogen, halo, acetamido, allyloxy, thiophenyl, sulfoxyalkyl, or sulfoxyphenyl.

18. (New) A compound according to claim 1 selected from:

